

Module Five: Clinical Considerations

Total time for this module: 4 hours

Training Objectives

- Participants will review TB transmission, diagnosis and treatment.
- Participants will learn the differences in TB clinical, microbiologic, and radiographic presentation in HIV-infected patients.
- Participants will review the treatment of patients with HIV-associated TB.
- Participants will review prevention and early treatment of opportunistic infections among HIV-infected patients and the use of antiretroviral therapy (ARV).
- Participants will understand how to prevent HIV and TB transmission in the health facility.

Advance Preparation

- The best person to present Module Five is one who understands the medical issues related to TB treatment, HIV infection, and the management of patients infected with both HIV and TB. If the trainer does not have this background, consider a guest lecturer or have a knowledgeable person available to answer questions after the basic presentation.
- Prepare overheads (or use the PowerPoint presentation):
 - Overhead 5-1: Learning Objectives
 - Overhead 5-2: TB Infection and Disease
 - Overhead 5-3: Infection and Disease (2)
 - Overhead 5-4: Natural History of TB Infection – HIV Negative
 - Overhead 5-5: Natural History of TB Infection – HIV Positive
 - Overhead 5-6: Natural History of TB Disease – No Treatment Given
 - Overhead 5-7: Natural History of TB Disease – No Treatment Given (2)
 - Overhead 5-8: Diagnosis of Pulmonary TB
 - Overhead 5-9: Photograph - Preparing the Slides with Specimens
 - Overhead 5-10: Photograph - Laboratory Technician
 - Overhead 5-11: Photograph - Mycobacteria Under the Microscope.
 - Overhead 5-12: Diagnosis of Pulmonary TB (2)
 - Overhead 5-13: Radiographic Abnormalities Typical of Pulmonary TB
 - Overhead 5-14: Differential Diagnosis (Other Diseases Patient May Have)
 - Overhead 5-15: TB Treatment
 - Overhead 5-16: TB Treatment (2)
 - Overhead 5-17: Transmission of TB (Photograph)
 - Overhead 5-18: Review
 - Overhead 5-19: Differences in TB Clinical, Microbiologic and Radiographic Presentation in HIV-infected Patients: Learning Objectives
 - Overhead 5-20: Clinical Impact of CD4 Cell Decrease
 - Overhead 5-21: TB in Early Stages of HIV Infection
 - Overhead 5-22: TB in Later Stages of HIV Infection
 - Overhead 5-23: Clinical Manifestations: Sites of Involvement and HIV Status

Overhead 5-24: Proportion of Patients with Pulmonary TB Who Have Positive AFB Sputum Smears

Overhead 5-25: Effect of Stage of HIV Disease on Radiographic Manifestations of TB

Overhead 5-26: 5 X-Rays

Overhead 5-27: Review

Overhead 5-28: Treatment of Patients with HIV-associated TB: Learning Objectives

Overhead 5-29: Prevention and Early Treatment of Opportunistic Infections

Overhead 5-30: Antiretroviral Therapy (ARV)

Overhead 5-31: Antiretroviral Therapy

Overhead 5-32: Who Is Eligible for ARV Therapy?

Overhead 5-33: Issues in Using Antiretroviral Therapy During TB Therapy

Overhead 5-34: Association Between HIV Serostatus and Risk of Death during Treatment

Overhead 5-35: How Can Outcomes of HIV-related TB Be Improved?

Overhead 5-36: Directly observed therapy (DOT) for TB can have a major impact on the outcome of TB patients with HIV infection.

Overhead 5-37: Effect of Mode of Administration of TB Treatment on Outcome of HIV-related TB

Overhead 5-38: Antiretroviral (ARV) therapy can have a major impact on survival with TB in HIV-infected patients.

Overhead 5-39: Comparison of HIV Disease Progression With and Without ARV Therapy

Overhead 5-40: Identifying Patients Who Would Benefit from ARV during TB Therapy

Overhead 5-41: So why don't we start all HIV-infected TB patients on ARV?

Overhead 5-42: Issues in Using Antiretroviral Therapy During TB Therapy

Overhead 5-43: Drug-drug Interactions

Overhead 5-44: Drug-drug Interactions (2)

Overhead 5-45: Issues in Using Antiretroviral Therapy During TB Therapy

Overhead 5-46: Immune Reconstitution Inflammatory Syndrome

Overhead 5-47: Immune Reconstitution Inflammatory Syndrome (2)

Overhead 5-48: Risk Factors for the Development of Immune Reconstitution Events

Overhead 5-49: Management of Suspected Immune Reconstitution Inflammatory Syndrome

Overhead 5-50: Issues in Using Antiretroviral Therapy During TB Therapy

Overhead 5-51: Overlapping Anti-TB and ARV Drug Toxicities

Overhead 5-52: Overlapping Anti-TB and ARV Drug Toxicities (2)

Overhead 5-53: Management of Adverse Events During Treatment of HIV and TB

Overhead 5-54: Issues in Using Antiretroviral Therapy During TB Therapy

Overhead 5-55: Adherence with Treatment for TB and HIV

Overhead 5-56: Adherence with Treatment for TB and HIV (2)

Overhead 5-57: Review

Overhead 5-58: Prevention of HIV and TB Transmission in the Health Facility

Overhead 5-59: Prevention of Bloodborne Transmission

Overhead 5-60: Prevention of Airborne Transmission

Overview of Module Five

In Module Five, the trainer will discuss the difference between TB infection and disease and how TB is transmitted and diagnosed. The trainer will also discuss the relationship between TB and HIV. At the end of this module, there will be an opportunity for participants to ask questions on all the material covered in this training.

TB Infection and Disease

1:00 – 2:00 PM

Overhead 5-1

Learning Objectives

At the end of this presentation you will be able to:

- Describe the difference between TB infection and disease
- Describe how TB is transmitted
- Describe how TB is diagnosed

Overhead 5-1

Introduce the Module

In this presentation we are we are going to learn about TB infection and disease. We will discuss the difference between TB infection and disease, how TB is transmitted, and how TB is diagnosed. We will also discuss the relationship between TB and HIV.

TB Infection and Disease

Overhead 5-2

TB Infection and Disease

- Cause: *Mycobacterium tuberculosis*
- TB infection:
 - Person carries TB bacilli in the body
 - Small numbers of bacilli, dormant (sleeping)
 - No symptoms, not infectious
 - Globally: 2 billion people infected

Overhead 5-2

TB stands for tuberculosis. TB is caused by a bacterium (germ) called *Mycobacterium tuberculosis*.

It is important to understand the difference between TB infection and TB disease.

TB infection occurs when people carry TB in their bodies, but the TB bacterium (germ) is dormant or sleeping. Because the bacterium is dormant, these people will not have symptoms and are not infectious. Therefore they will not spread TB to others. Globally, about 2 billion people are infected with TB.

Overhead 5-3

Infection and Disease (2)

- TB disease:
 - Bacilli multiply
 - One or more organs diseased
 - Signs and symptoms like weight loss, chronic cough, coughing up blood, night sweats, fever
 - Pulmonary disease is infectious
 - Globally: > 8 million new cases each year

Overhead 5-3

In some people, the TB bacterium begins to multiply in one or more organs. When this happens, people develop signs and symptoms like weight loss, chronic cough, coughing up blood, night sweats, and fever.

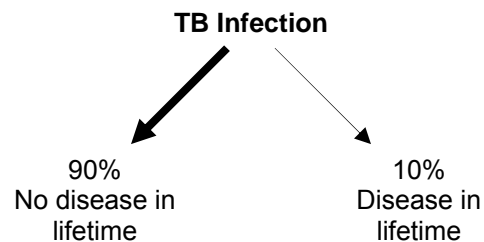
If they have pulmonary disease, which means it is in the lungs, they can spread TB infection to others.

Globally, over 8 million new cases of TB disease occur each year.

**Natural History
of TB Infection**

Overhead 5-4

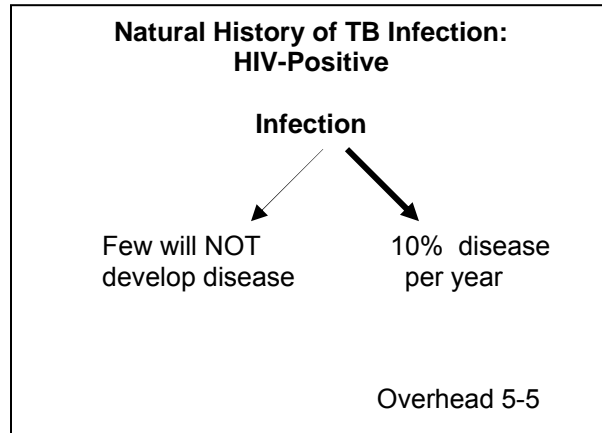
**Natural History of TB Infection:
HIV-Negative**



Overhead 5-4

“Natural history” refers to the course of TB infection if no therapy is given. Even without therapy, only about 10% of people who become infected with TB will develop TB disease in a lifetime. 90% of people will never develop TB disease.

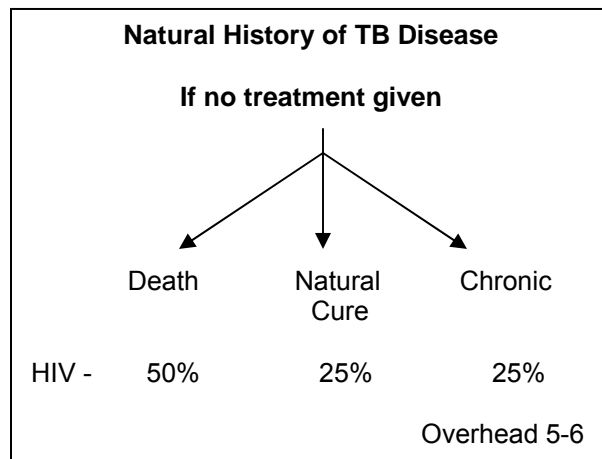
Overhead 5-5



However, this is **NOT** the case in people who are HIV-infected. In this case, about 10% of HIV-infected patients with TB infection will develop TB disease each year. Only a few HIV-infected TB patients will never develop TB disease.

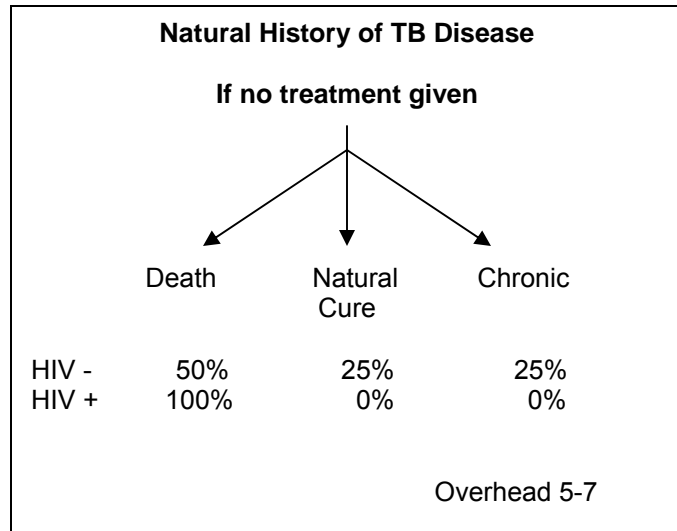
Thus, TB infection in HIV patients is a serious problem.

Overhead 5-6



In patients with TB disease who **DO NOT** have HIV, about 50% will die if no treatment is given; 25% will be cured even without treatment; and 25% will develop chronic disease.

Overhead 5-7

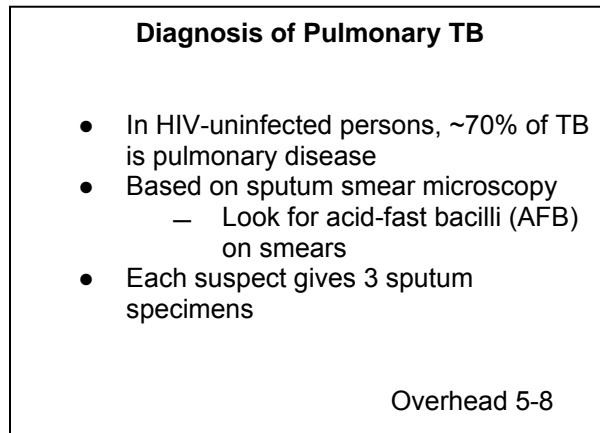


However, in patients with TB disease who DO have HIV infection, note that 100% (all) will die.

Again, TB is a serious disease in HIV-infected patients.

Pulmonary TB

Overhead 5-8



In HIV-uninfected persons, about 70% of TB is pulmonary disease. TB is diagnosed based on sputum smear microscopy, looking for acid-fast bacilli (AFB) on smears.

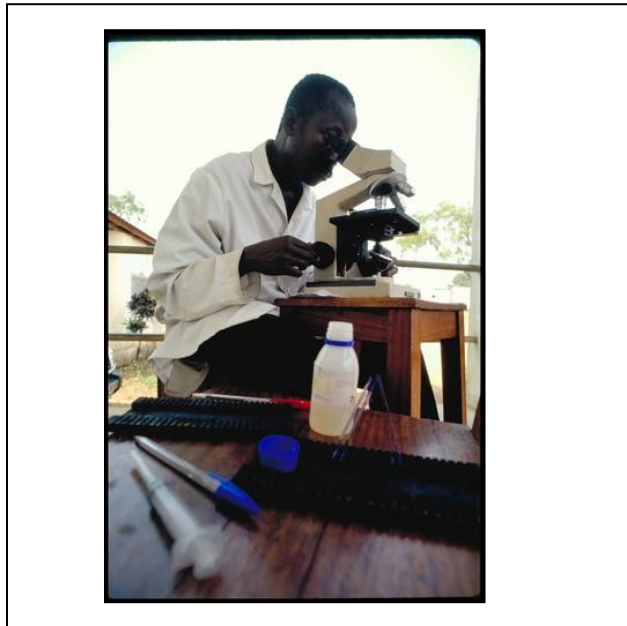
Each suspect patient gives 3 sputum specimens. At least 2 smears showing AFB bacilli from 3 specimens indicates “smear positive TB.”

Overhead 5-9



This picture shows the microscopy laboratory preparing the slides with sputum specimens collected from the TB suspects.

Overhead 5-10



This is a picture of a laboratory technician looking at sputum smears under the microscope.

Overhead 5-11



This slide shows how the mycobacteria look under the microscope.

However, not all TB patients can be diagnosed by looking at sputum smears. There must be a concentration of 5 to 10 thousand mycobacteria in a cubic milliliter of sputum to detect the bacterium under best conditions of microscopy.

By contrast, bacterial culture will detect TB if there is a concentration of 10 to 100 per ml.

Detection of TB by sputum smears in HIV-infected patients may be very difficult because these patients tend to have fewer mycobacteria in their sputum.

Overhead 5-12

Diagnosis of Pulmonary TB (2)

Algorithm for diagnosis of smear-negative TB:

- Chest radiography
- If not consistent with TB:
 - course of broad spectrum antibiotics
- If no resolution in symptoms
 - repeat sputum smears
 - clinical judgment

Overhead 5-12

If the sputum smear is positive, then a clear diagnosis of TB can be made and patients are started on treatment. In cases of suspect TB when sputum smears are negative, a chest x-ray may be helpful in making the diagnosis. If the chest x-ray is not consistent with TB, then the patient should be treated with a course of broad spectrum antibiotics. If there is no resolution of the symptoms, then repeat sputum smears and use clinical judgment as to whether to treat for TB.

The lecturer should determine the standard protocol for AFB smear-negative suspects of the national TB program, and describe that protocol if it is different from the one described above.

Overhead 5-13

Radiographic Abnormalities Typical of Pulmonary TB

- Upper lobe infiltrate
- Cavitation
- Pulmonary fibrosis and shrinkage

Overhead 5-13

Typical radiographic abnormalities of pulmonary TB include upper lobe infiltrate, cavitation, and pulmonary fibrosis and shrinkage.

Overhead 5-14

**Differential Diagnosis
(Other Diseases Patient May Have)**

- Bronchiectasis
- Cancer – lung cancer, lymphoma or Kaposi's sarcoma of lung
- Lung abscess
- *Pneumocystis jiroveci* pneumonia
- Bacterial or fungal pneumonia
- Congestive heart failure
- Asthma
- Chronic obstructive airways disease

Other diseases that could cause similar findings on the x-ray include:

- Bronchiectasis
- Cancer – lung cancer, lymphoma or Kaposi's sarcoma of lung
- Lung abscess
- *Pneumocystis jiroveci* pneumonia
- Bacterial or fungal pneumonia
- Congestive heart failure
- Asthma
- Chronic obstructive airways disease

TB Treatment

Overhead 5-15

TB Treatment

- Standardized treatment regimens (WHO Clinical Manual p. 116)
- Short course regimens: 6-8 months
- Two phases
 - Intensive phase: to kill most bacilli
 - Continuation phase: to sterilize
- Directly observed therapy

Overhead 5-15

Fortunately, TB can be treated successfully. There are standardized treatment regimens recommended by WHO. A cure can be obtained in 6-8 months using short course regimens.

There are 2 phases to treatment:

- An intensive phase during which most bacilli are killed
- A continuation phase to be sure that all bacilli are killed

Patients who do not always take their TB medications can develop resistant bacilli and will not be cured. Thus, TB control programs use something called “directly observed therapy” to make sure that all patients take their medications. Directly observed therapy means that the providers watch their patients take their drugs for each dose.

Overhead 5-16

TB Treatment

- First line drugs (WHO Clinical Manual p. 112)
 - INH or H – isoniazid
 - RIF or R – rifampicin
 - ETH or E – ethambutol
 - PYZ or Z – pyrazinamide
 - STR or S – streptomycin
- Drugs may be separate or in fixed-dose combinations (FDC)

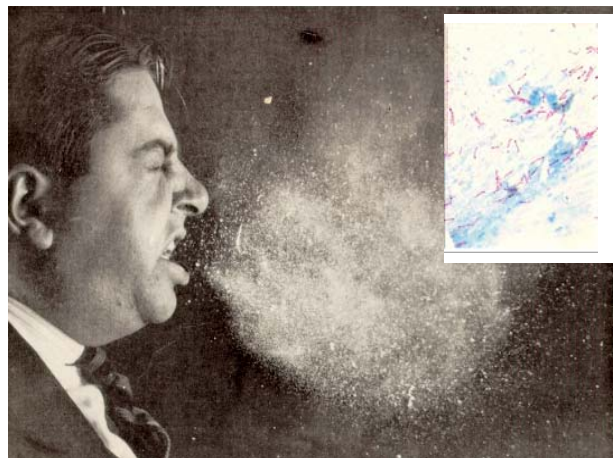
Overhead 5-16

The first line drugs (WHO Clinical Manual p. 112) for TB include:

INH	or H	– isoniazid
RIF	or R	– rifampicin
ETH	or E	– ethambutol
PYZ	or Z	– pyrazinamide
STR	or S	– streptomycin

Drugs may be given separately or in fixed-dose combinations (FDC).

Overhead 5-17



Overhead 5-17

TB is transmitted through the air. When a person with untreated TB of the lungs coughs, he expels droplets of sputum containing *M. tuberculosis* into the air. These droplets cannot usually be seen. Someone else can breathe in these droplets and thus become infected with *M. tuberculosis*. In general it takes days or weeks of exposure to air contaminated with these droplets to become infected. Remember we talked earlier about how HIV can be transmitted. HIV cannot be transmitted through the air like TB can.

Review

Overhead 5-18

Review

- What is the difference between TB infection and disease?
- How is TB transmitted?
- How is pulmonary TB diagnosed?

Overhead 5-18

Let's review what we have just covered.

Trainer should ask the questions in the overhead and get responses from the participants before going on to the next section.

Differences in TB Clinical, Microbiologic and Radiographic Presentation in HIV-infected Patients

2:00 – 2:40 PM

Overhead 5-19

Learning Objectives

At the end of this presentation, you will be able to:

- Describe the association between the stage of HIV/AIDS and the clinical/microbiologic/radiographic manifestations of TB
- Summarize why it is more difficult to diagnose HIV-related TB than non-HIV TB
- Describe how HIV changes the clinical, microbiologic and radiographic manifestations of TB

Overhead 5-19

At the end of this presentation, you will be able to:

- Describe the association between the stage of HIV/AIDS and the clinical/microbiologic/radiographic manifestations of TB
- Summarize why it is more difficult to diagnose HIV-related TB than non-HIV TB
- Describe how HIV changes the clinical, microbiologic and radiographic manifestations of TB

Effect of Immune Suppression on TB

Overhead 5-20

Clinical Impact of CD4 Cell Decrease

- Accelerated progression from recent TB infection to active disease
- Increased rates of reactivation of latent TB of up to 10% per year
- Increased risk for re-infection and subsequent recurrent disease

Overhead 5-20

How does the immune suppression (CD4 decline) affect TB?
HIV-immune suppressed patients can rapidly develop TB if they become infected. In other words, the time between TB infection and TB disease is decreased.

There are increased rates of reactivation. Up to 10% of people with both HIV infection and TB infection will develop TB disease each year.

Immune-suppressed patients are at increased risk for re-infection with TB and subsequent recurrent disease.

Overhead 5-21

TB in Early Stages of HIV Infection

- Typical of TB in immuno-competent persons
 - Usually localized to lung
 - Usually upper lobes of lung
 - Often with cavitation on chest radiograph
 - Usually AFB sputum smear positive

Overhead 5-21

As you will recall, HIV-infected patients are not immune-suppressed in the early stages of the disease. TB disease in these patients, therefore, is very much like typical TB disease in patients without HIV infection.

Remember that typical TB disease has these characteristics:

- Usually localized to lung
- Usually upper lobes of lung
- Often with cavitation on chest radiograph
- Usually AFB sputum smear positive

Overhead 5-22

TB in Later Stages of HIV Infection

- Clinical
 - more extrapulmonary TB
 - alone or in combination with pulmonary
- Microscopy in pulmonary disease
 - often AFB sputum smear negative
- Chest radiograph in pulmonary disease
 - mid or lower lobe or hilar (area around heart shadow) involvement

Overhead 5-22

However, as HIV-infected patients progress to immunosuppression, their TB disease will become more atypical. From the clinical perspective, these patients will have more extrapulmonary TB, either alone or in combination with pulmonary TB.

Clinical Manifestations

With HIV-immune suppression, the sputum smears are often smear negative, making diagnosis difficult. The chest x-rays may also be atypical with mid- or lower-lobe or hilar involvement.

Overhead 5-23

Clinical Manifestations: Sites of Involvement and HIV Status

Site	HIV-positive (%)	HIV-negative (%)
Pulmonary	40	72
Extrapulmonary	34	16
Both	26	12
Pleural	31	19
Lymph node	19	3

J Trop Med Hygiene 1993

Overhead 5-23

This study in the *Journal of Tropical Medicine Hygiene* compared the sites of TB involvement in HIV-positive and negative patients. The proportions do not add up to 100% because some patients have both pulmonary and extrapulmonary TB.

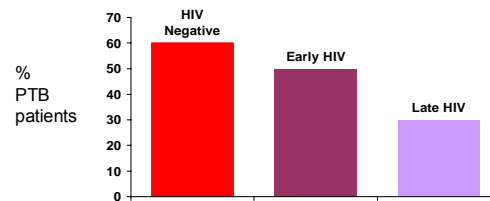
As you can see, the HIV-positive patients had less pulmonary involvement compared with HIV-negative patients: 40% vs 72%.

HIV-positive patients were more likely to have extrapulmonary disease; the most common kinds of extrapulmonary disease are pleural TB and lymph node TB—

- extrapulmonary disease: 34% vs 16%
- pleural involvement: 31% vs 19%
- AND lymph node involvement: 19% vs 3%

Overhead 5-24

Proportion of Patients with Pulmonary TB Who Have Positive AFB Sputum Smears



Overhead 5-24

As I mentioned earlier, HIV-infected patients are less likely to have positive sputum smears for TB. Note in this study that about 60% of HIV-negative patients had positive sputum smears; only 50% of those with early HIV disease had positive smears; and only about 30% with late HIV disease had positive smears.

Overhead 5-25

**Effect of Stage of HIV Disease on
Radiographic Manifestations of TB**

Early HIV disease

- Upper lobe predominance
- Cavitation
- Pleural disease

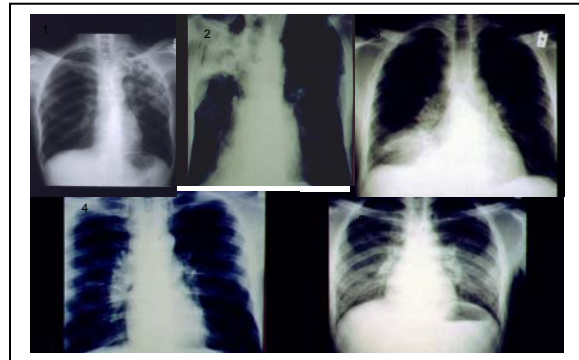
Advanced HIV disease

- Lack of cavitation
- Hilar adenopathy
- Lower and middle lobe infiltrates
- Pleural and pericardial involvement

Overhead 5-25

As we saw earlier, HIV immune suppression also has an effect on the radiographic manifestations of TB. Note that in early HIV disease, the typical findings are seen: upper lobe predominance, cavitation, and pleural disease. While in advanced HIV disease, there are more atypical findings: lack of cavitation, hilar adenopathy, lower and middle lobe infiltrates, and pleural and pericardial involvement.

Overhead 5-26



In x-ray number 1, there is an infiltrate and cavitation in the upper lobe on the left.

In number 2, there is scarring from old TB disease in the upper right lobe. The scarring and fibrosis have made the right lobe much smaller than a healthy lung.

These first two chest x-rays are typical findings in pulmonary TB.

The other three chest x-rays show the way TB can look in patients with HIV-related immunosuppression. Number 3 shows a right lower lobe infiltrate; number 4, hilar adenopathy; and number 5, bilateral infiltrates.

Review

Overhead 5-27

Review

- How does HIV change the clinical, microbiologic, and radiographic manifestations of TB?
- What is the association between the stage of HIV/AIDS and the clinical/microbiologic/radiographic manifestations of TB?
- Why is it more difficult to diagnose HIV-related TB than non-HIV TB?

Overhead 5-27

Let's review what we have just covered.

Trainer should ask the questions in the overhead and get responses from the participants before going on to the next section.

Break
2:40 – 3:00 PM

Take a 20 minute break.

Treatment of Patients with HIV-associated TB

3:00 – 4:30 PM

Overhead 5-28

Learning Objectives

At the end of this presentation you will be able to:

- Describe the treatment for HIV infection
- Describe which TB patients would benefit most from early initiation of ARV therapy
- Name 4 challenges to managing patients on anti-TB and ARV therapy
- Describe the key to managing patients on TB and ARV therapy

Overhead 5-28

In this next presentation, we will cover a number of topics related to the treatment of patients with TB and HIV infection. At the end of the presentation, you will be able to:

- Describe the treatment for HIV infection
- Describe which TB patients would benefit most from early initiation of ARV therapy
- Name 4 challenges to managing patients on anti-TB and ARV therapy
- Describe the key to managing patients on TB and ARV therapy

Cotrimoxazole Prophylaxis

Overhead 5-29

Prevention and Early Treatment of Opportunistic Infections

- Cotrimoxazole prophylaxis
 - Trimethoprim-sulfamethoxazole or TMP/SMX
 - 46% reduction in mortality
 - Lower rates of malaria, diarrhea, bacterial pneumonia, hospital admissions
 - Evolving guidelines on which adults and children should receive TMP/SMX (WHO Clinical Manual p.181)

Overhead 5-29

Mermin et al, Lancet 2004

On the first day of this training, we talked about opportunistic infections or OIs associated with HIV infection. TB is one of the opportunistic infections that we talked about. One of the ways that OIs can be prevented is by giving an antibiotic called cotrimoxazole to HIV-infected patients. This drug is sometimes called cotrim, or bactrim, or TXP-SMX, or trimethoprim-sulfamethaxazole. Giving this drug to the patient is called prophylaxis because the drug is given before the patient becomes ill.

Antiretroviral Therapy (ARV)

A study by Mermin and colleagues in Uganda has shown a 46% reduction in mortality when this drug is given to HIV-infected patients. Lower rates of malaria, diarrhea, bacterial pneumonia, and hospital admissions were also observed during the study. WHO is formulating guidelines on which adults and children with HIV should receive this drug.

Overhead 5-30

Antiretroviral Therapy (ARV)

- Stops HIV virus from multiplying in the body
- Amount of virus (viral load) decreases
- CD4 cell count increases
- Immune function improves

Overhead 5-30

As we have said earlier, HIV is a virus. It is a special type of virus called “retrovirus”. Therefore, treatment for HIV disease is called antiretroviral therapy. “Anti” means “against.” Antiretroviral is often abbreviated as ARV. ARV drugs stop HIV from multiplying in the body. When these drugs are given to patients, their viral load decreases and their CD4 cell counts increase. Immune function improves.

Overhead 5-31

Antiretroviral Therapy

- First line ARV therapy – 3 drugs
 - Stavudine (d4T) or Zidovudine (ZDT)
 - Lamivudine (3TC)
 - Nevirapine (NVP) or Efavirenz (EVF)
- Sometimes single dose NVP used to prevent mother-to-child transmission

Overhead 5-31

ARV drugs are NEVER given one at a time, but ALWAYS in combination. The first time patients are given ARV therapy, they are given 3 drugs: stavudine or zidovudine, lamivudine, and either nevirapine or efavirenz. The only time that any ARVs are given alone is in some regimens to prevent mother-to-child transmission.

Pregnant women can be given a single dose of nevirapine to reduce their risk of transmitting HIV to their baby.

Overhead 5-32

Who Is Eligible for ARV Therapy?

- WHO has recommended the following, but eligibility criteria vary by country.
- WHO stage IV regardless of CD4 count
- WHO stage III with consideration of using CD4 cell counts >200 but $<350/\text{mm}^3$ to assist decision-making
- All patients with CD4 $<200/\text{mm}^3$

Overhead 5-32

Not all HIV-infected patients must be treated at the time of diagnosis. In fact, treatment with ARVs is not given until patients reach the later stages of illness. WHO guidelines recommend (*can substitute your national guidelines if different*):

- Patients with WHO stage IV disease are treated regardless of CD4 cell counts.
- Patients with WHO stage III disease who have CD4 counts <350 cells per cubic millimeter should be considered for treatment.
- All patients with CD4 counts <200 should be treated.

Overhead 5-33

Issues in Using Antiretroviral Therapy during TB Therapy

- Identifying patients who would benefit from antiretroviral therapy
- Drug-drug interactions
- Immune reconstitution events
- Overlapping drug side effect profiles
- Adherence challenge of multidrug therapy for 2 diseases

Overhead 5-33

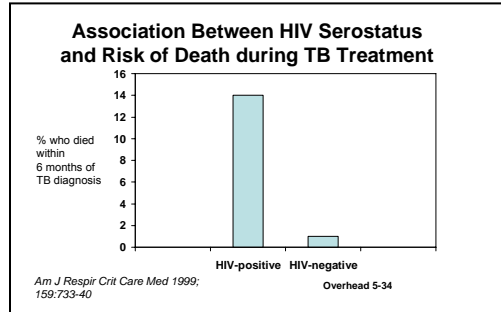
Some of the issues in using ARVs during TB therapy are:

- Identifying patients who would benefit from antiretroviral therapy
- Drug-drug interactions
- Immune reconstitution events
- Overlapping drug side effect profiles
- Adherence challenge of multidrug therapy for 2 diseases

We will discuss these in more detail in this presentation.

HIV Status of TB Patients and Risk of Death

Overhead 5-34



TB patients with HIV are much more likely to die of TB than HIV-negative TB patients. As can be seen from this slide, about 14% of HIV-positive patients in this study conducted in South Africa died while less than 2% of HIV-negative patients died.

Overhead 5-35

How Can Outcomes of HIV-related TB Be Improved?

- Early diagnosis of TB
- Appropriate treatment of TB
- Assure adherence with TB treatment (use of directly observed therapy, DOT)
- Use of cotrimoxazole in all TB patients
- Use of ART to treat HIV in selected patients

Overhead 5-35

How can outcomes of HIV-related TB be improved?

- **Early diagnosis of TB**
- **Appropriate treatment of TB**
- **Assure adherence with TB treatment by using directly observed therapy or DOT**
- **Use of cotrimoxazole in all TB patients**
- **Use of ART to treat HIV in selected patients**

Overhead 5-36

Directly observed therapy (DOT) for TB can have a major impact on the outcome of TB patients with HIV infection.

Overhead 5-36

It is very important that patients adhere to the regimen of TB treatment. Therefore, directly observed therapy for TB can have a major impact on the outcome of TB patients with HIV infection. This next slide shows the impact that DOT can have on patient outcome.

Overhead 5-37

Effect of Mode of Administration of TB Treatment on Outcome of HIV-related TB		
Outcome	DOT	Self-administered
Alive	85%	57%
Died from TB	10%	37%
Died, not due to TB	4%	7%

AIDS 1994;8:1103-8

Overhead 5-37

In this study in the United States, 85% of HIV-infected TB patients undergoing DOT were alive at the end of TB treatment vs. only 57% of those who self-administered. Among those who self-administered, 37% died vs. only 10% of the DOT patients. Among the self-administered patients, 7% died of other causes vs. 4% among the DOT patients.

Overhead 5-38

Antiretroviral (ARV) therapy can have a major impact on survival with TB in HIV-infected patients.

Overhead 5-38

Clearly, antiretroviral or ARV therapy can have a major impact on the survival of HIV-infected patients with TB.

Overhead 5-39

Comparison of HIV Disease Progression With and Without ARV Therapy		
	No ARV	ARV
Years of enrollment	1993-1995	1999-2003
Baseline CD4 cell count	85/mm ³	90/mm ³
Proportion patients who used ARV during TB rx	0%	80%
Death within 1 year of starting TB therapy	20%	5%
Death or new OI within 1 year of starting TB therapy	39%	16%
<small>Burman et al, CROI 2003</small>		
<small>Overhead 5-39</small>		

In this US-based study, some patients received ARVs (right column), while others did not (left column). As you can see, the baseline CD4 counts were similar: 85 cells per cubic millimeter in the left column versus 90 cells per cubic millimeter in the right column. This indicates that the patients in both groups had the same degree of immunosuppression.

However, among the patients who received ARVs, only 5% died within 1 year of starting TB therapy, while 20% of those who did not receive ARVs died within one year. Among the patients receiving ARVs, only 16% died of a new opportunistic infection (OI) vs. 39% of those who did not receive ARVs.

Overhead 5-40

Identifying Patients Who Would Benefit from ARV during TB Therapy ⁽²⁾
<ul style="list-style-type: none">• Laboratory (CD4 cell count < 350)• Clinical criteria (extrapulmonary TB)• Both identify patients at increased risk for HIV disease progression or death during TB treatment who would benefit from ARV
<small>Overhead 5-40</small>

Not all TB patients with HIV infection should be treated with ARVs. The clinical criteria that HIV-infected TB patients should have for starting ARVs are either determined by laboratory test—a CD4 cell count < 350 or by the clinical criteria, extrapulmonary TB.

Both low CD4 count and extrapulmonary TB identify patients at increased risk for HIV disease progression or death during TB treatment who would benefit from ARV.

Overhead 5-41

**So why don't we start all HIV-
infected TB patients on ARV?**

Overhead 5-41

So why don't we start all HIV-infected TB patients on ARV?

Overhead 5-42

**Issues in Using Antiretroviral
Therapy During TB Therapy**

- **Drug-drug interactions**
- Immune reconstitution inflammatory syndrome - IRIS
- Overlapping drug side effect profiles
- Adherence challenge of multidrug therapy for 2 diseases

Overhead 5-42

There are several issues that need to be considered when using ARVs during TB therapy:

First, the drugs for both HIV and TB interact and dosages may need to be adjusted.

Second, as the immune system improves with ARV therapy, it can temporarily make the TB disease worse. This is called immune reconstitution inflammatory syndrome, or IRIS.

There are overlapping drug side effects.

Finally, adhering to both the TB and HIV regimens can be a challenge for patients.

We will discuss each of these issues in detail in the next few slides.

Issues...

**Drug-drug
Interactions**

Overhead 5-43

Drug-drug Interactions

- Patients on rifampin have altered ARV drug metabolism.
- NVP and certain other ARVs cannot be used with rifampicin.
- Some other ARV drug dosages must be adjusted.

Overhead 5-43

What are the drug interactions?

- Patients on rifampicin have altered ARV drug metabolism.
- NVP and certain other ARVs cannot be used with rifampicin.
- Some other ARV drug dosages must be adjusted.

Overhead 5-44

Drug-drug Interactions ⁽²⁾

SOLUTION:
COMMUNICATION AND
COORDINATION between TB and
HIV treatment providers

Overhead 5-44

TB and HIV treatment providers must know what drugs the patient is taking, when they are starting and stopping. They must communicate and coordinate care.

Issues...

**Immune
Reconstitution
Inflammatory
Syndrome**

Overhead 5-45

**Issues in Using Antiretroviral
Therapy During TB Therapy**

- Drug-drug interactions
- **Immune reconstitution inflammatory syndrome**
- Overlapping drug side effect profiles
- Adherence challenge of multidrug therapy for 2 diseases

Overhead 5-45

Now let's talk about immune reconstitution inflammatory syndrome.

Overhead 5-46

**Immune Reconstitution
Inflammatory Syndrome**

- Temporary worsening of TB symptoms, signs or radiographic findings
- Occurs within days to weeks of starting ARV
- Rarely associated with starting TB therapy
- Natural history
 - Duration: days to months
 - Waxing and waning is common.

Overhead 5-46

The improvement in the immune system in patients taking ARVs can cause a temporary worsening of TB symptoms, signs, or radiographic findings. This is called immune reconstitution inflammatory syndrome. These events occur within days to weeks of starting ARVs.

These events are rarely associated with starting TB therapy alone. Immune reconstitution events can last days to months and can wax and wane in their severity.

Overhead 5-47

**Immune Reconstitution
Inflammatory Syndrome ⁽²⁾**

- High fevers
- Enlarging lymph nodes
- New or expanding central nervous system lesions
- Worsening of pulmonary infiltrates, including respiratory failure
- Worsening meningitis

Overhead 5-47

These are the signs and symptoms of immune reconstitution:

- High fevers
- Enlarging lymph nodes
- New or expanding central nervous system lesions
- Worsening of pulmonary infiltrates, including respiratory failure
- Worsening meningitis

In some series more than one-third of TB patients started on ARV had these reactions.

Overhead 5-48

Risk Factors for the Development of Immune Reconstitution Events

- Low CD4 cell count
- Shorter time from the initiation of TB therapy to the initiation of antiretroviral therapy

Overhead 48

Patients with lower CD4 counts are more likely to develop immune reconstitution events.

Also, when the time between initiation of TB therapy and the initiation of HIV therapy is short, these patients are more likely to develop immune reconstitution events.

Overhead 5-49

Management of Suspected Immune Reconstitution Inflammatory Syndrome

- Inform patients about the possibility of an event after starting ARV. ("You may feel like the TB is coming back.")
- Evaluate for possible TB treatment failure.
- Assess for other HIV-related complications, e.g., another opportunistic infection.
- Use non-steroidal anti-inflammatory drugs for symptoms
- Steroids may be needed for severe symptoms.

Overhead 5-49

How should these patients be managed?

- **Inform patients about the possibility of an event occurring after they start ARV. ("You may feel like the TB is coming back.")**
- **Evaluate for possible TB treatment failure.**
- **Assess for other HIV-related complications, e.g., another opportunistic infection.**
- **Use non-steroidal anti-inflammatory drugs for symptoms.**
- **Steroids may be needed for severe symptoms.**

Issues...

Overlapping Drug Side Effects

Overhead 5-50

Issues in Using Antiretroviral Therapy During TB Therapy

- Drug-drug interactions
- Immune reconstitution events
- **Overlapping drug side effect profiles**
- Adherence challenge of multidrug therapy for 2 diseases

Overhead 5-50

Now let's talk about overlapping drug side effects.

Overhead 5-51

Overlapping Anti-TB and ARV Drug Toxicities

Side Effect	Possible Causes	
	Anti-TB Drugs	ARV Drugs
Skin rash	INH, RIF, PZA	NVP, DVP, EFV
Nausea, vomiting	INH, RIF, PZA	ZDV, RTV, IDV
Hepatitis	INH, RIF, PZA	NVP, Pls
Leukopenia, anemia	RIF	ZDV

Overhead 5-51

ARVs and TB drugs can cause many of the same side effects. If patients are taking both types of drugs, providers can have a very difficult time deciding on which drug is causing the side effect.

This slide lists common side effects and notes which ARVs and TB drugs cause these effects. As you can see, there is a lot of overlap.

The ARV drugs highlighted in bold are first line ARV treatment.

Overhead 5-52

Overlapping Anti-TB and ARV Drug Toxicities ⁽²⁾

**SOLUTION: COMMUNICATION AND
COORDINATION** between TB and HIV
treatment providers

- Start HIV and TB therapies separately
 - Example 1: For patients with a CD4 count < 100, start TB treatment, wait 2 weeks, start HIV treatment
 - Example 2: For patients with a CD4 count > 100, start TB treatment, wait 2 months, start HIV treatment

Overhead 5-52

The solution to this problem is communication and coordination between TB and HIV treatment providers. Some of the confusion can be avoided by doing one thing at a time. For instance, instead of starting both therapies at the same time, start each therapy separately. One example of this separate therapy model would be: for patients with a CD4 count less than 100, start TB treatment, wait 2

weeks, then start ART; and for patients with a CD4 count higher than 100, start TB treatment, wait 2 months, then start ART.

Overhead 5-53

**Management of Adverse Events
During Treatment of HIV and TB**

- Stop all medications for severe adverse events.
- Use sequential re-challenge to decide the cause of an event.
- Don't change from the first-line TB drugs (especially INH and RIF) without evidence of an association with a significant side effect.

Overhead 5-53

How should these side effects be managed?

- **Stop all medications, including TB medications, for severe adverse events.**
- **Use sequential re-challenge to decide the cause of an event.**
- **Don't change from the first-line TB drugs (especially INH and RIF) without evidence of an association with a significant side effect.**

Issues...

**Treatment
Adherence
for TB and
HIV**

Overhead 5-54

**Issues in Using Antiretroviral
Therapy During TB Therapy**

- Drug-drug interactions
- Immune reconstitution events
- Overlapping drug side effect profiles
- **Adherence challenge of multidrug therapy for 2 diseases**

Overhead 5-54

Now let's talk about the challenges patients face in taking both types of drugs.

Overhead 5-55

**Adherence with Treatment for
TB and HIV**

- Establish a close relationship between the TB and HIV/AIDS treatment program.
- Make sure patient is ready for antiretroviral therapy – multiple new medications, chance of overlapping adverse events, more complicated than once-daily TB treatment.

Overhead 5-55

Taking lots of medications can be quite challenging for patients. The treatment for both diseases requires taking drugs for a long period of time. To help patients, providers should:

- Establish a close relationship between the TB and HIV/AIDS treatment program.
- Make sure patient is ready for antiretroviral therapy. Remember that there will be multiple new medications, a chance of overlapping adverse events, and the patient's treatment is more complicated than once-daily TB treatment.

Overhead 5-56

**Adherence with Treatment for
TB and HIV ⁽²⁾**

- TB treatment often uses directly observed therapy (DOT) – if possible, use DOT visits to enhance adherence to antiretroviral therapy as well.
- Try to coordinate medication pick-ups.

Overhead 5-56

TB treatment often uses directly observed therapy (DOT) – if possible, use DOT visits to enhance adherence to antiretroviral therapy as well.

Try to coordinate medication pick-ups.

Review

Overhead 5-57

Review

- Which patients would benefit from initiation of ARV therapy during TB treatment?
- What are the major challenges to managing patients on anti-TB and ARV therapy?
- What is the key to managing patients on TB and ARV therapy?

Overhead 5-57

Let's review what we have just covered.

Trainer should ask the questions in the overhead and get responses from the participants before going on to the next section.

Prevention of HIV and TB Transmission in the Health Facility

4:30 – 5:00 PM

We will finish this module by reviewing ways to prevent the transmission of HIV and TB in the health facility.

Overhead 5-58

Prevention of HIV and TB Transmission in the Health Facility

- HIV transmission is bloodborne (in the health facility)
 - After needle-stick injury, risk is < 1 in 200. (data from US)
- TB transmission is airborne
 - Incidence of TB in HCW significantly higher than that in general population in some studies.

Overhead 1-19

As we have discussed, HIV transmission is bloodborne in the healthcare facility. This means that HIV can be transmitted to a healthcare worker through accidental needle-sticks with needles that have been contaminated with blood from an HIV-infected patient. These needle-stick accidents can often happen while drawing blood from an infected patient.

Fortunately the risk of transmission from a needle-stick injury is very low, <1 out of 200 sticks, based on data from the United States.

TB transmission, on the other hand, is airborne. Transmission of TB to healthcare workers is not rare. The incidence of TB in healthcare workers is significantly higher than that in the general population in some studies.

Prevention of Bloodborne Transmission

Overhead 5-59

Prevention of Bloodborne Transmission

- Wear latex gloves when performing venipuncture or giving injection.
- Do not re-cap needles.
- Dispose of "sharps" in puncture-resistant disposal containers.
- Keep containers near point of use.
- Avoid unnecessary injections.

Overhead 5-59

Even though transmission of HIV in the healthcare setting is rare, precautions need to be taken. These precautions include:

- Wear latex gloves when performing venipuncture or giving injection.

***Prevention of
Airborne
Transmission***

- Do not re-cap needles.
- Dispose of “sharps” in puncture-resistant disposal containers.
- Keep containers near point of use.
- Avoid unnecessary injections.

Overhead 5-60

**Prevention of Airborne
Transmission**

- Workplace or administrative controls
 - Early detection and rapid evaluation of TB suspects
 - Appropriate treatment after TB diagnosis
 - Cough triage – ask patients in waiting area about cough; place coughing patients in separate waiting area
- Environmental controls
 - Maximize natural ventilation in waiting areas and examining rooms

Overhead 5-60

To prevent airborne transmission of diseases such as TB, workplace or administrative guidelines include:

- Early detection and rapid evaluation of TB suspects, so that these patients can be put on treatment quickly and moved to areas of the clinic or hospital that are designed to prevent spread of disease.
- Appropriate treatment after TB diagnosis is important to make the patient noninfectious in the shortest time possible.
- Cough triage – ask patients in waiting area about cough; place coughing patients in separate waiting area so they don’t spread infection to others.

Environmental controls should also be in place: Maximize natural ventilation in waiting areas and examining rooms.

WHO has published guidelines for TB infection control in health care settings which can be obtained from their web page on the Internet.

Conclusion

This concludes Module Five on clinical considerations when treating TB patients who are also HIV-infected.

Are there any questions?

Trainer should answer any questions participants have.

Instruct participants to return in the morning for a final interactive session that will require their new skills and knowledge.

Overheads

Module 5: Clinical Considerations

Learning Objectives

At the end of this module, you will be able to:

- Describe the difference between TB infection and disease
- Describe how TB is transmitted
- Describe how TB is diagnosed

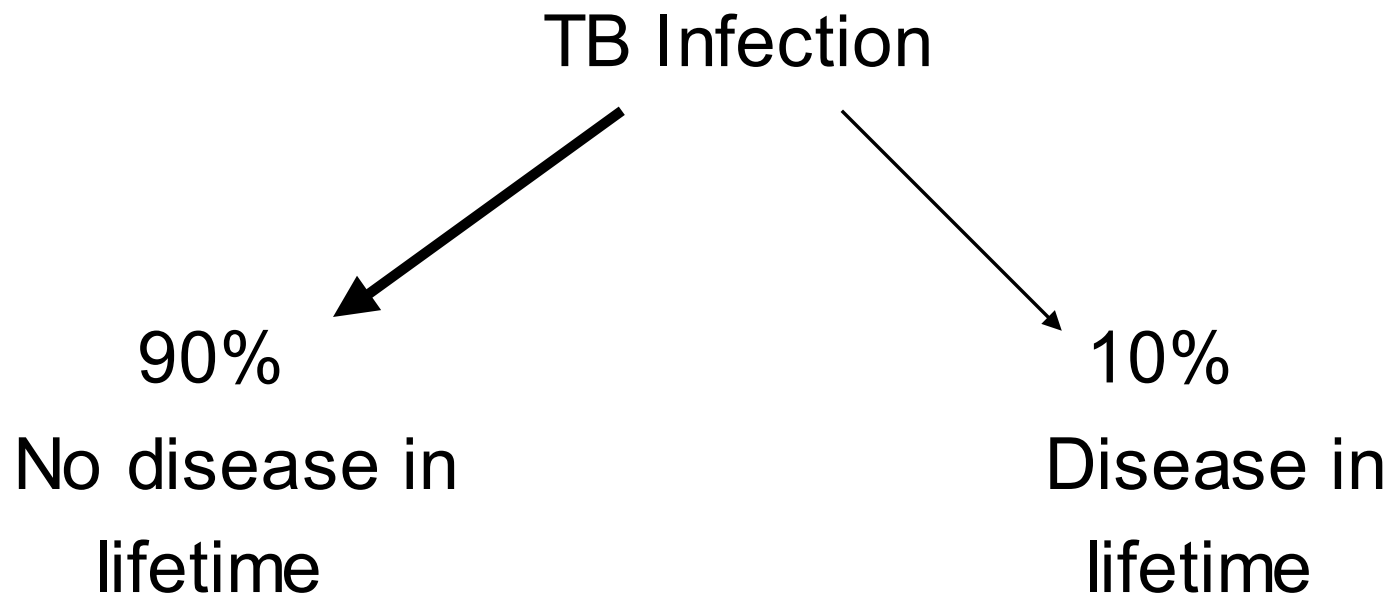
TB Infection and Disease

- Cause: *Mycobacterium tuberculosis*
- TB infection:
 - Person carries TB bacilli in the body
 - Small numbers of bacilli, dormant (sleeping)
 - No symptoms, not infectious
 - Globally: 2 billion people infected

Infection and Disease ⁽²⁾

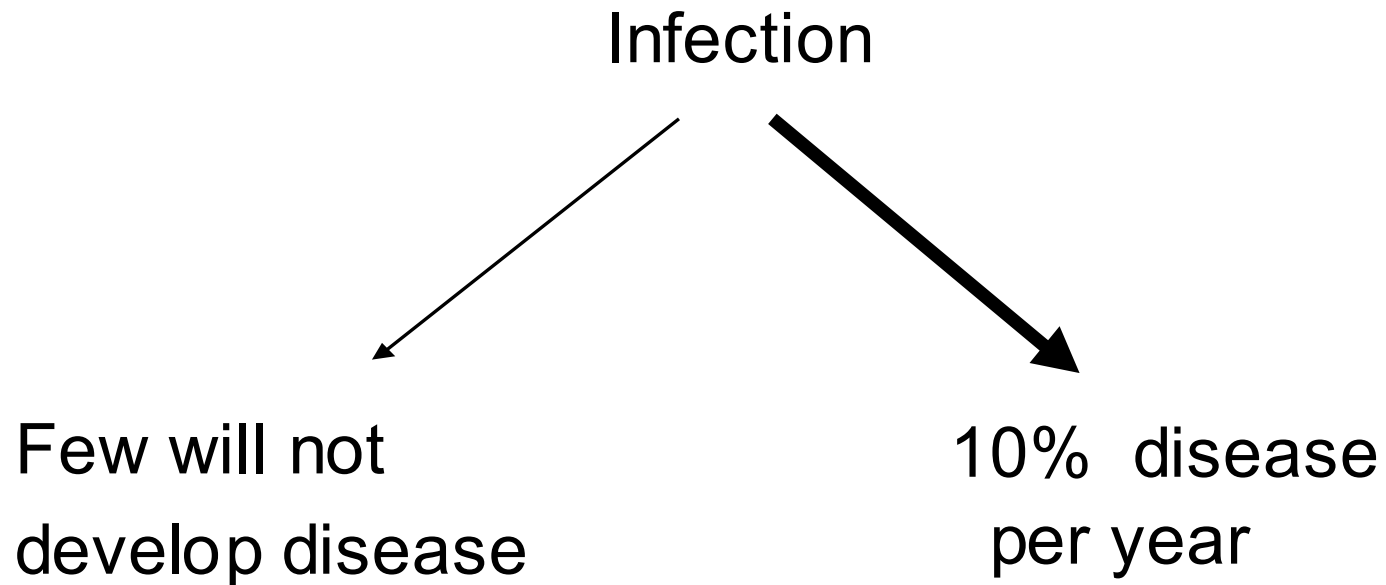
- TB disease:
 - Bacilli multiply
 - One or more organs diseased
 - Signs and symptoms like weight loss, chronic cough, coughing up blood, night sweats, fever
 - Pulmonary disease is infectious
 - Globally: > 8 million new cases each year

Natural History of TB Infection – HIV Negative



Overhead 5-4

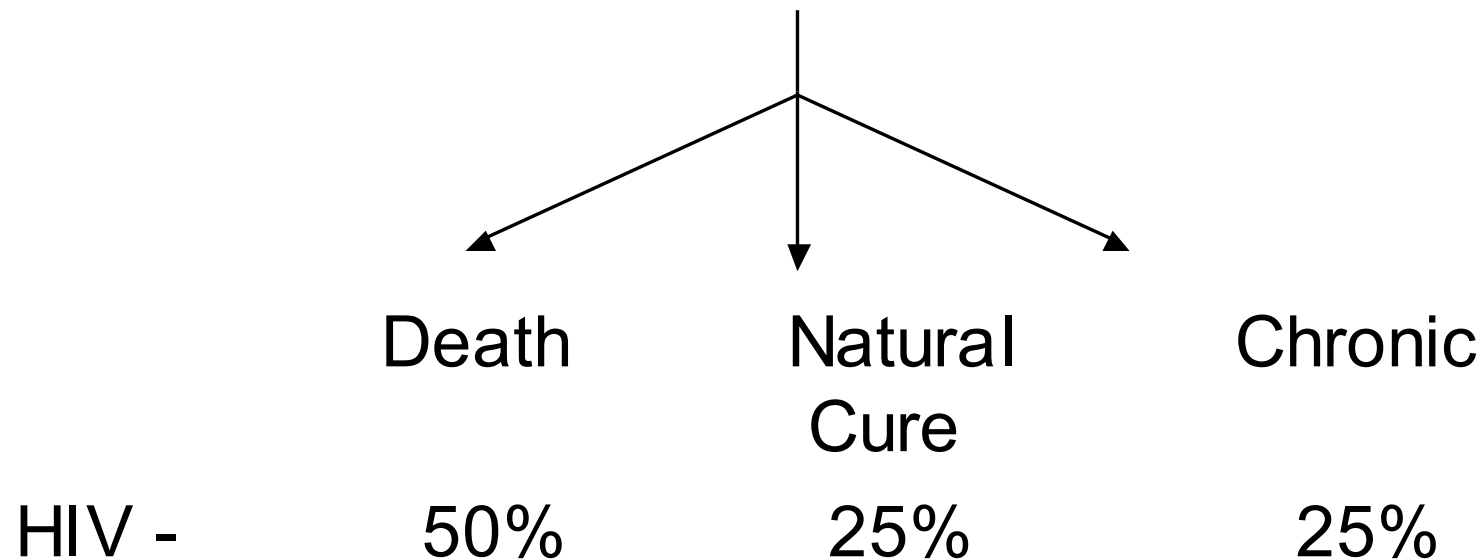
Natural History of TB Infection – HIV Positive



Overhead 5-5

Natural History of TB Disease

If no treatment given

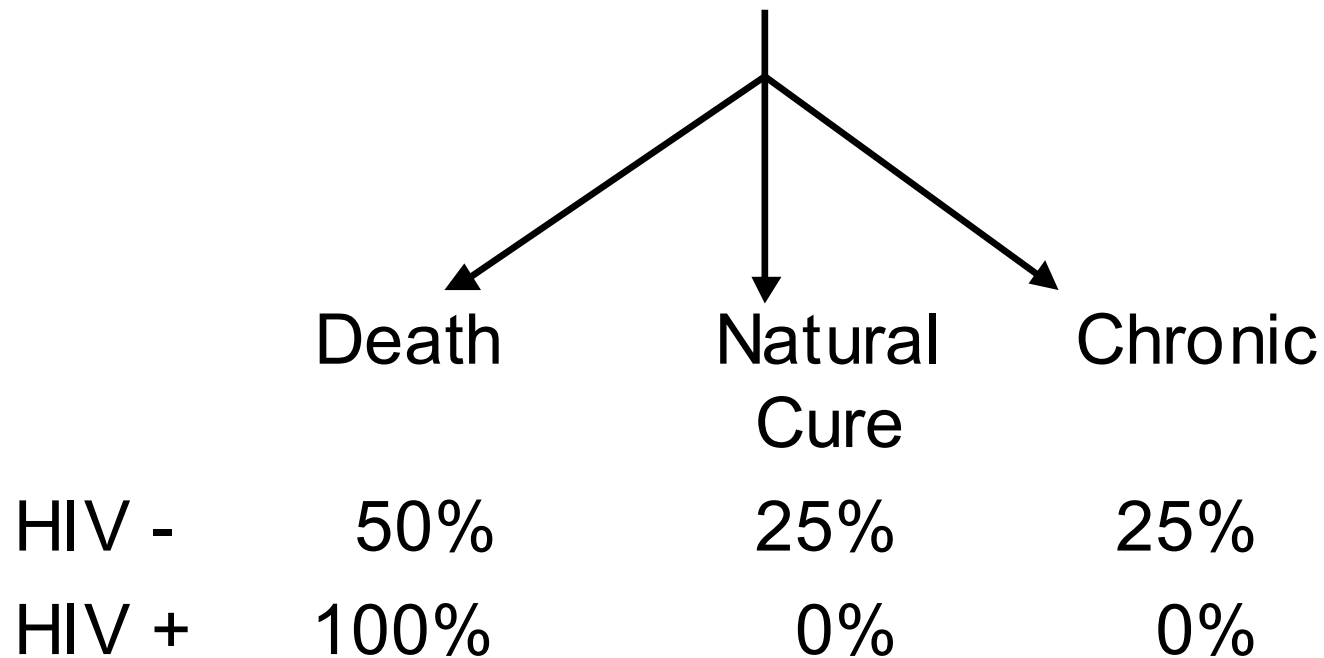


HIV -

Overhead 5-6

Natural History of TB Disease

If no treatment given



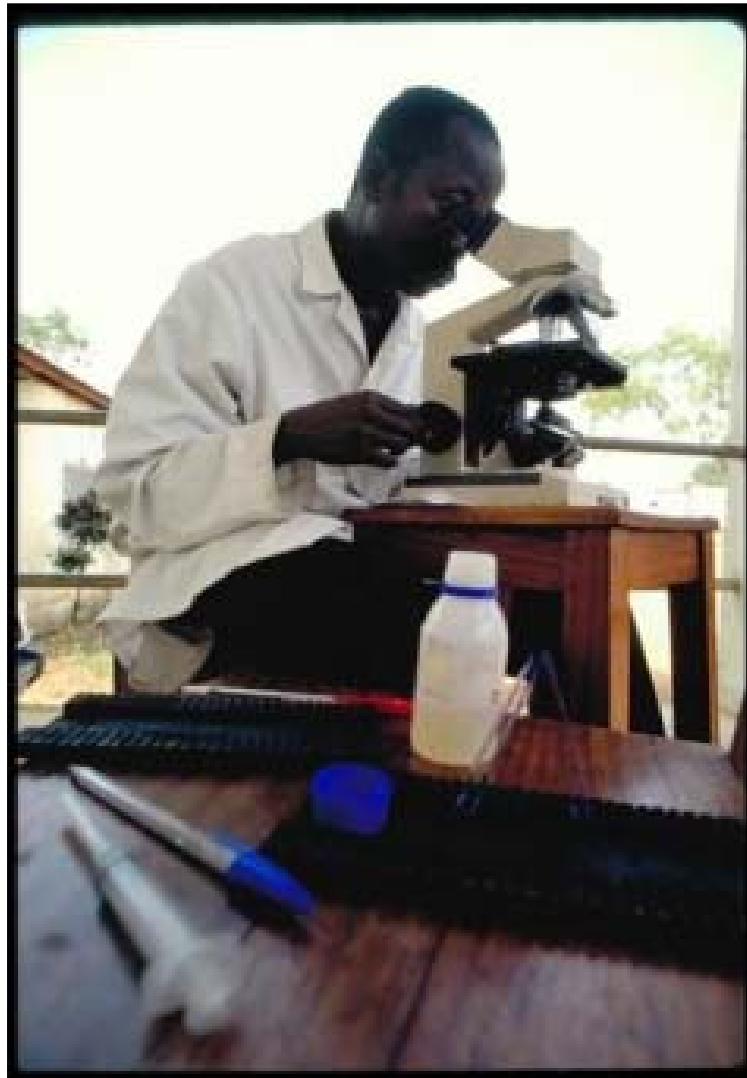
Overhead 5-7

Diagnosis of Pulmonary TB

- In HIV-uninfected persons, ~70% of TB is pulmonary disease
- Based on sputum smear microscopy
 - Look for acid-fast bacilli (AFB) on smears
- Each suspect gives 3 sputum specimens

Overhead 5-8





Overhead 5-10



Overhead 5-11

Diagnosis of Pulmonary TB ⁽²⁾

Algorithm for diagnosis of smear-negative TB:

- Chest radiography
- If not consistent with TB:
 - course of broad spectrum antibiotics
- If no resolution in symptoms
 - repeat sputum smears
 - clinical judgment

Overhead 5-12

Radiographic Abnormalities Typical of Pulmonary TB

- **Upper lobe infiltrate**
- **Cavitation**
- **Pulmonary fibrosis and shrinkage**

Differential Diagnosis (Other Diseases Patient May Have)

- Bronchiectasis
- Bronchial carcinoma
- Lung abscess
- *Pneumocystis carinii* pneumonia
- Congestive heart failure
- Asthma
- Chronic obstructive airways disease

Overhead 5-14

TB Treatment

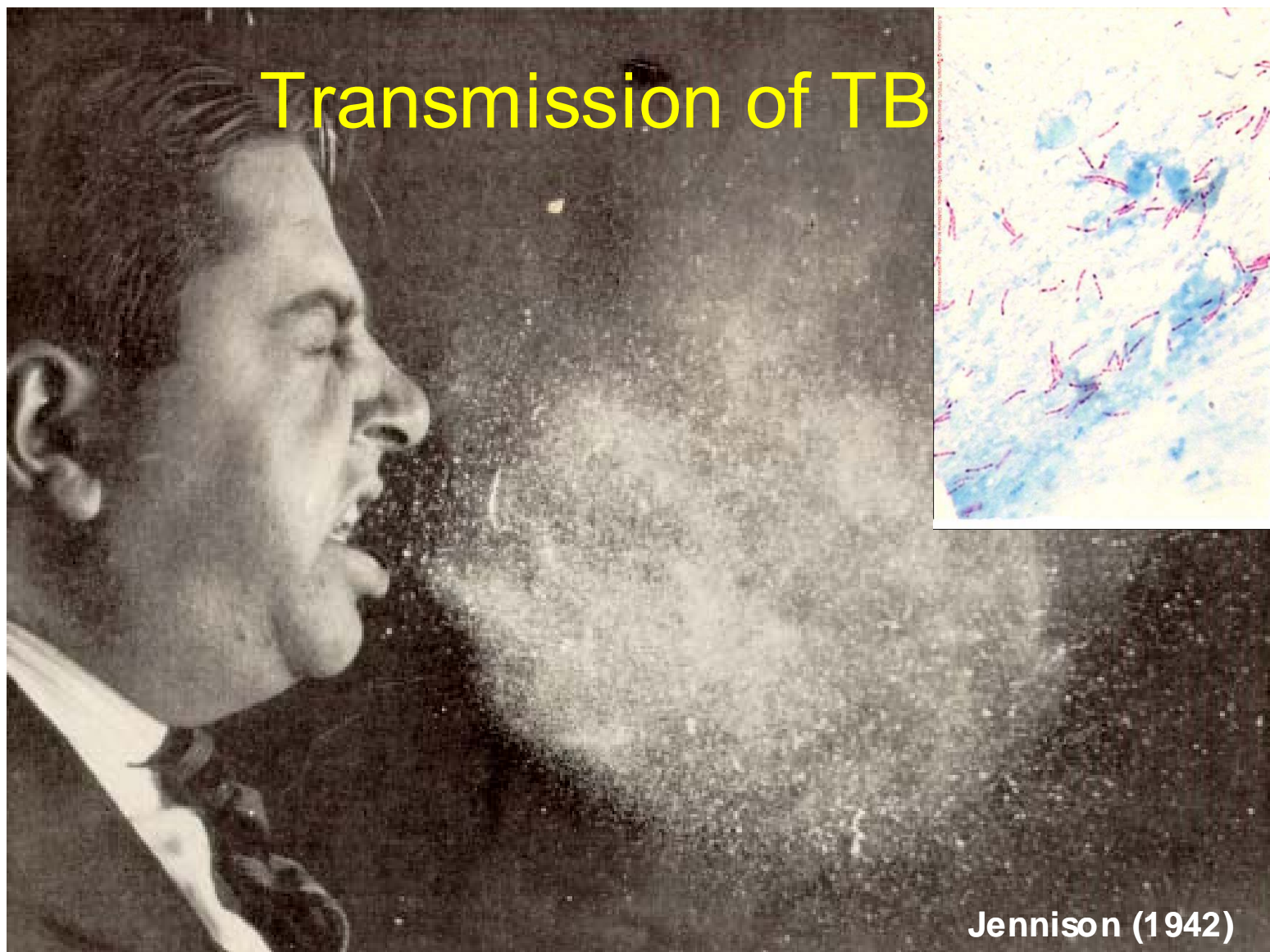
- Standardized treatment regimens (WHO Clinical Manual p. 116)
- Short course regimens: 6-8 months
- Two phases
 - Intensive phase: to kill most bacilli
 - Continuation phase: to sterilize
- Directly observed therapy

Overhead 5-15

TB Treatment

- First line drugs (WHO Clinical Manual p112)
 - INH or H – isoniazid
 - RIF or R – rifampicin
 - ETH or E – ethambutol
 - PYZ or Z – pyrazinamide
 - STR or S – streptomycin
- Drugs may be separate or in fixed-dose combinations (FDC)

Transmission of TB



Overhead 5-17

Review

- What is the difference between TB infection and disease?
- How is TB transmitted?
- How is pulmonary TB diagnosed?

Learning Objectives

At the end of this presentation, you will be able to:

- Describe the association between the stage of HIV/AIDS and the clinical/microbiologic/radiographic manifestations of TB
- Summarize why it is more difficult to diagnose HIV-related TB than non-HIV TB
- Describe how HIV changes the clinical, microbiologic and radiographic manifestations of TB

Clinical Impact of CD4 Cell Decrease

- Accelerated progression from recent TB infection to active disease
- Increased rates of reactivation of latent TB of up to 10% per year
- Increased risk for re-infection and subsequent recurrent disease

TB in Early Stages of HIV Infection

- Typical of TB in immuno-competent persons
 - Usually localized to lung
 - Usually upper lobes of lung
 - Often with cavitation on chest radiograph
 - Usually AFB sputum smear positive

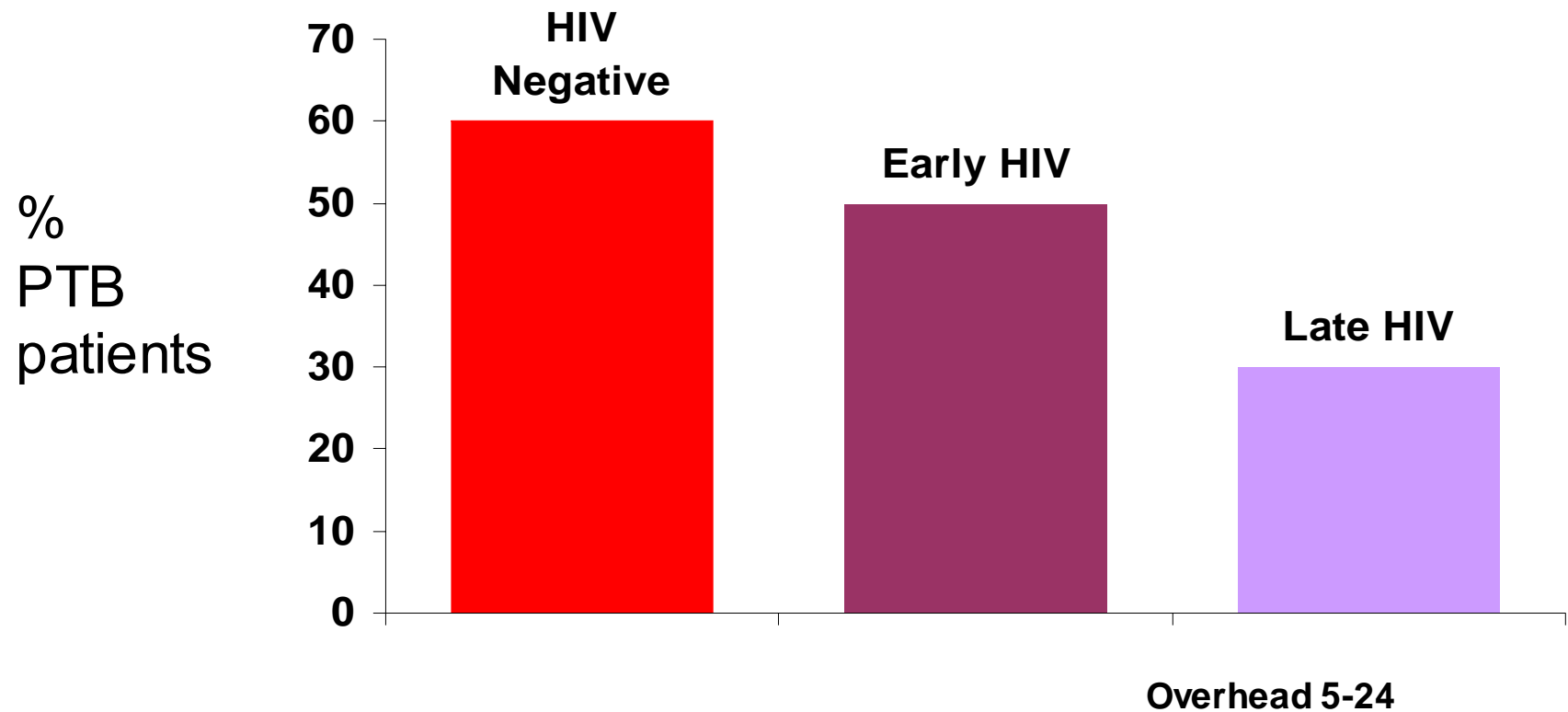
TB in Later Stages of HIV Infection

- Clinical
 - more extrapulmonary TB
 - alone or in combination with pulmonary
- Microscopy in pulmonary disease
 - often AFB sputum smear negative
- Chest radiograph in pulmonary disease
 - mid or lower lobe or hilar (area around heart shadow) involvement

Clinical Manifestations: Sites of Involvement and HIV Status

Site	HIV-positive (%)	HIV-negative (%)
Pulmonary	40	72
Extrapulmonary	34	16
Both	26	12
Pleural	31	19
Lymph node	19	3

Proportion of Patients with Pulmonary TB Who Have Positive AFB Sputum Smears



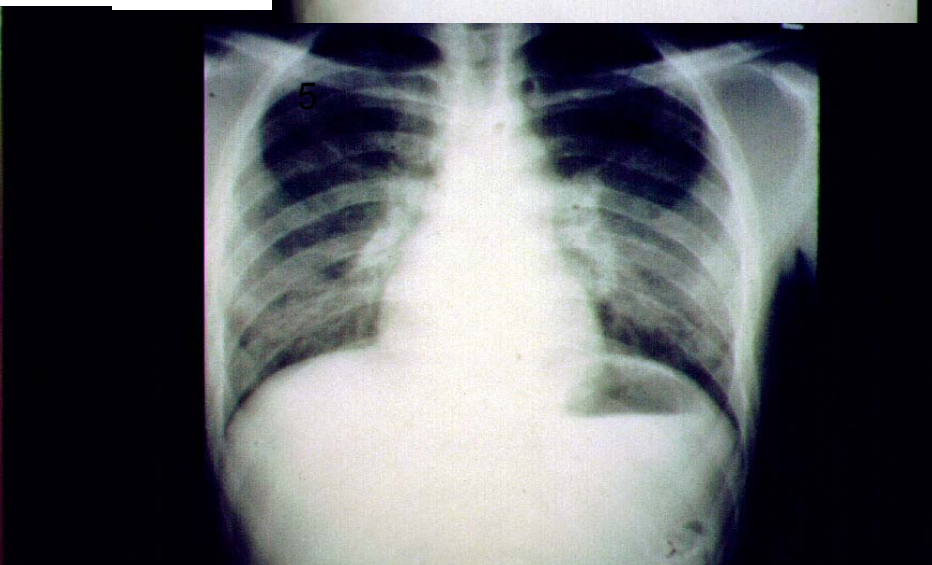
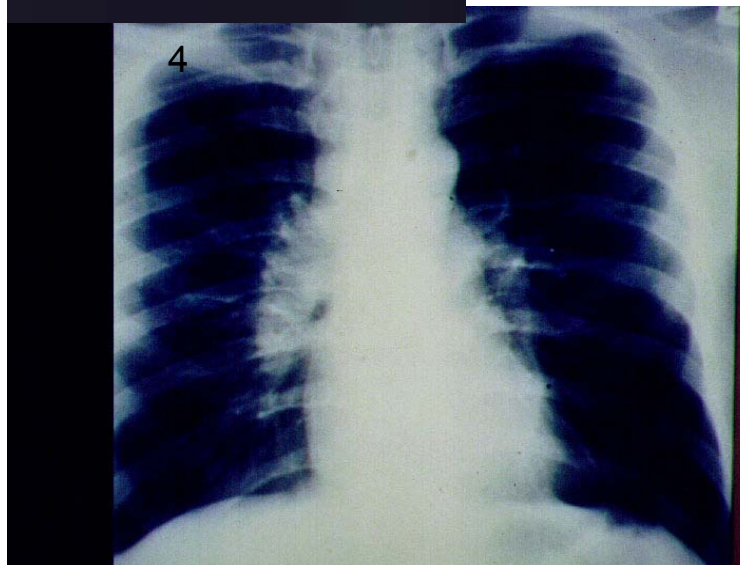
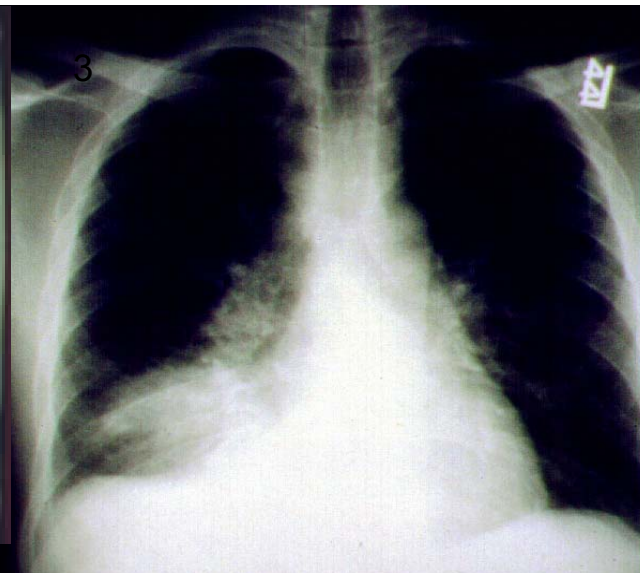
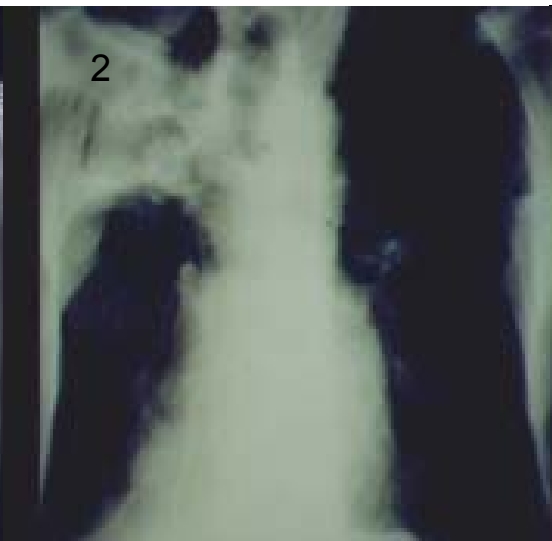
Effect of Stage of HIV Disease on Radiographic Manifestations of TB

Early HIV disease

- Upper lobe predominance
- Cavitation
- Pleural disease

Advanced HIV disease

- Lack of cavitation
- Hilar adenopathy
- Lower and middle lobe infiltrates
- Pleural and pericardial involvement



Review

- How does HIV change the clinical, microbiologic and radiographic manifestations of TB?
- What is the association between the stage of HIV/AIDS and the clinical/microbiologic/radiographic manifestations of TB?
- Why is it more difficult to diagnose HIV-related TB than non-HIV TB?

Learning Objectives

At the end of this presentation you will be able to:

- Describe the treatment for HIV infection
- Describe which TB patients would benefit most from early initiation of ARV therapy
- Name 4 challenges to managing patients on anti-TB and ARV therapy
- Describe the key to managing patients on TB and ARV therapy

Prevention and Early Treatment of Opportunistic Infections

- Cotrimoxazole prophylaxis
 - Trimethoprim-sulfamethoxazole or TMP/SMP
 - 46% reduction in mortality
 - Lower rates of malaria, diarrhea, bacterial pneumonia, hospital admissions
 - Evolving guidelines on which adults and children should receive TMP/SMP (WHO Clinical Manual p.181)

Overhead 5-29

Mermin et al, Lancet 2004

Antiretroviral Therapy (ARV)

- Stops HIV virus from multiplying in the body
- Amount of virus (viral load) decreases
- CD4 cell count increases
- Immune function improves

Antiretroviral Therapy

- First line ARV therapy – 3 drugs
 - Stavudine (d4T) or Zidovudine (ZDT)
 - Lamivudine (3TC)
 - Nevirapine (NVP) or Efavirenz (EVF)
- Sometimes single dose NVP used to prevent mother-to-child transmission

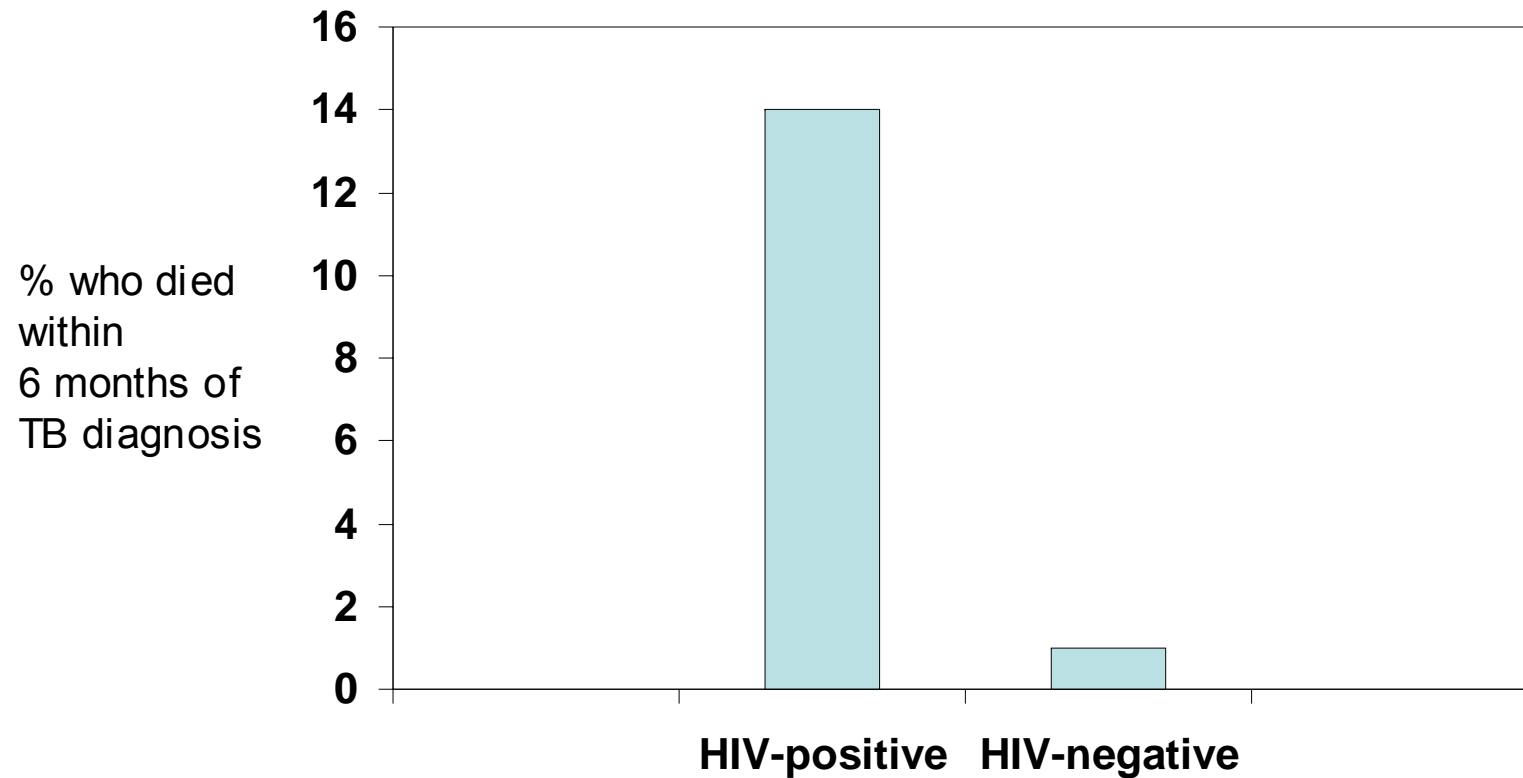
Who Is Eligible for ARV Therapy?

- WHO stage IV regardless of CD4 count
- WHO stage III with consideration of using CD4 cell counts >200 but $<350/\text{mm}^3$ to assist decision-making
- All patients with CD4 $<200/\text{mm}$

Issues in Using Antiretroviral Therapy during TB Therapy

- Identifying patients who would benefit from antiretroviral therapy
- Drug-drug interactions
- Immune reconstitution events
- Overlapping drug side effect profiles
- Adherence challenge of multidrug therapy for 2 diseases

Association Between HIV Serostatus and Risk of Death during TB Treatment



Am J Respir Crit Care Med 1999;
158:733-40

Overhead 5-34

How Can Outcomes of HIV-related TB Be Improved?

- Early diagnosis of TB
- Appropriate treatment of TB
- Assure adherence with TB treatment (use of directly observed therapy, DOT)
- Use of cotrimoxazole in all TB patients
- Use of ART to treat HIV in selected patients

**Directly observed therapy (DOT)
for TB can have a major impact
on the outcome of TB patients
with HIV infection.**

Effect of Mode of Administration of TB Treatment on Outcome of HIV-related TB

Outcome	DOT	Self-administered
Alive	85%	57%
Died from TB	10%	37%
Died, not due to TB	4%	7%

Overhead 5-37

AIDS 1994;8:1103-8

Antiretroviral (ARV) therapy can have a major impact on survival with TB in HIV-infected patients.

Comparison of HIV Disease Progression With and Without ARV Therapy

	No ARV	ARV
Years of enrollment	1993-1995	1999-2003
Baseline CD4 cell count	85/mm ³	90/mm ³
Proportion patients who used ARV during TB rx	0%	80%
Death within 1 year of starting TB therapy	20%	5%
Death or new OI within 1 year of starting TB therapy	39%	16%

Identifying Patients Who Would Benefit from ARV during TB Therapy ⁽²⁾

- Laboratory (CD4 cell count < 350)
- Clinical criteria (extrapulmonary TB)
- Both identify patients at increased risk for HIV disease progression or death during TB treatment who would benefit from ARV

So why don't we start all HIV-infected TB patients on ARV?

Overhead 5-41

Issues in Using Antiretroviral Therapy During TB Therapy

- **Drug-drug interactions** Immune reconstitution inflammatory syndrome - IRIS
- Overlapping drug side effect profiles
- Adherence challenge of multidrug therapy for 2 diseases

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Drug-drug Interactions

- Patients on rifampin have altered ARV drug metabolism.
- NVP and certain other ARVs cannot be used with rifampicin.
- Some other ARV drug dosages must be adjusted.

Drug-drug Interactions ⁽²⁾

SOLUTION:

**COMMUNICATION AND
COORDINATION between TB and
HIV treatment providers**

Issues in Using Antiretroviral Therapy During TB Therapy

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- Temporary worsening of TB symptoms, signs or radiographic findings
- Occurs within days to weeks of starting ARV
- Rarely associated with starting TB therapy
- Natural history
 - **Duration: days to months**
 - **Waxing and waning is common.**

Immune Reconstitution Inflammatory Syndrome ⁽²⁾

- High fevers
- Enlarging lymph nodes
- Expanding central nervous system lesions
- Worsening of pulmonary infiltrates, including respiratory failure
- Intracranial tuberculomas, worsening meningitis

Risk Factors for the Development of Immune Reconstitution Events

- Low CD4 cell count
- Shorter time from the initiation of TB therapy to the initiation of antiretroviral therapy

Management of Suspected Immune Reconstitution Inflammatory Syndrome

- Inform patients about the possibility of an event after starting ARV. (“You may feel like the TB is coming back.”)
- Evaluate for possible TB treatment failure.
- Assess for other HIV-related complications, e.g., another opportunistic infection.
- Use non-steroidal anti-inflammatory drugs for symptoms
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Overhead 5-50

Overlapping Anti-TB and ARV Drug Toxicities

Side Effect	<i>Possible Causes</i>	
	Anti-TB Drugs	ARV Drugs
Skin rash	INH, RIF, PZA	NVP , DVP, EFV
Nausea, vomiting	INH, RIF, PZA	ZDV , RTV, IDV
Hepatitis	INH, RIF, PZA	NVP , Pls
Leukopenia, anemia	RIF	ZDV

Overlapping Anti-TB and ARV Drug Toxicities ⁽²⁾

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- Stop all medications for severe adverse events.
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Adherence with Treatment for TB and HIV

- Establish a close relationship between the TB and HIV/AIDS treatment program.
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Overhead 5-55

Adherence with Treatment for TB and HIV ⁽²⁾

- TB treatment often uses directly observed therapy (DOT) – if possible, use DOT visits to enhance adherence to antiretroviral therapy as well.
- Try to coordinate medication pick-ups.

Review

- Which patients would benefit from initiation of ARV therapy during TB treatment?
- What are the major challenges to managing patients on anti-TB and ARV therapy
- What is the key to managing patients on TB and ARV therapy?

Prevention of HIV and TB Transmission in the Health Facility

- HIV transmission is bloodborne (in the health facility).
 - After needle-stick injury, risk is < 1 in 200.
(data from US)
- TB transmission is airborne.
 - Incidence of TB in HCW > 10 times that in general population in some studies.

Prevention of Bloodborne Transmission

- Wear latex gloves when performing venipuncture or giving injection.
- Do not re-cap needles.
- Dispose of “sharps” in puncture-resistant disposal containers.
- Keep containers near point of use.
- Avoid unnecessary injections.

Prevention of Airborne Transmission

- Workplace or administrative controls
 - Early detection and rapid evaluation of TB suspects
 - Appropriate treatment after TB diagnosis
 - Cough triage – ask patients in waiting area about cough; place coughing patients in separate waiting area
- Environmental controls
 - Maximize natural ventilation in waiting areas and examining rooms